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PATENT COOPERATION TREATY

PCT

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INTERNATIONAL PRELIMINARY EXAMINATION REPORT

(PCT Article 36 and Rule 70)

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Applicant's or agent's file reference ISIS-3267	FOR FURTHER ACTION	See Notification of Transmittal of International Preliminary Examination Report (Form PCT/IPEA/416)
International application No. PCT/US98/19199	International filing date *(day/month/year)* 16 SEPTEMBER 1998	Priority date *(day/month/year)* 16 SEPTEMBER 1997
International Patent Classification (IPC) or national classification and IPC IPC(6): A61K 37/00 and US Cl.: 514/2		
Applicant NIELSEN, PETER E.		

1. This international preliminary examination report has been prepared by this International Preliminary Examining Authority and is transmitted to the applicant according to Article 36.

2. This REPORT consists of a total of 5 sheets.

   [✓] This report is also accompanied by ANNEXES, i.e., sheets of the description, claims and/or drawings which have been amended and are the basis for this report and/or sheets containing rectifications made before this Authority. (see Rule 70.16 and Section 607 of the Administrative Instructions under the PCT).

   These annexes consist of a total of 4 sheets.

3. This report contains indications relating to the following items:

   I [X] Basis of the report

   II [ ] Priority

   III [ ] Non-establishment of report with regard to novelty, inventive step or industrial applicability

   IV [ ] Lack of unity of invention

   V [X] Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

   VI [ ] Certain documents cited

   VII [X] Certain defects in the international application

   VIII [ ] Certain observations on the international application

Date of submission of the demand	Date of completion of this report
15 APRIL 1999	10 DECEMBER 1999
Name and mailing address of the IPEA/US Commissioner of Patents and Trademarks Box PCT Washington, D.C. 20231 Facsimile No. (703) 305-3230	Authorized officer ARDIN MARSCHEL Telephone No. (703) 308-0196

Form PCT/IPEA/409 (cover sheet) (January 1994)*

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No.
PCT/US98/19199

I. Basis of the report

1. This report has been drawn on the basis of (*Substitute sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to the report since they do not contain amendments*):

☐ the international application as originally filed.

☒ the description, pages (See Attached) , as originally filed.
pages _____ , filed with the demand.
pages _____ , filed with the letter of _____.
pages _____ , filed with the letter of _____.

☒ the claims, Nos. (See Attached) , as originally filed.
Nos. _____ , as amended under Article 19.
Nos. _____ , filed with the demand.
Nos. _____ , filed with the letter of _____.
Nos. _____ , filed with the letter of _____.

☒ the drawings, sheets/~~fig~~ (See Attached) , as originally filed.
sheets/~~fig~~ _____ , filed with the demand.
sheets/~~fig~~ _____ , filed with the letter of _____.
sheets/~~fig~~ _____ , filed with the letter of _____.

2. The amendments have resulted in the cancellation of:

☒ the description, pages NONE.

☒ the claims, Nos. 1-22.

☒ the drawings, sheets/~~fig~~ NONE.

3. ☐ This report has been established as if (some of) the amendments had not been made, since they have been considered to go beyond the disclosure as filed, as indicated in the ~~Supplemental Box~~ Additional observations below (Rule 70.2(c)).

4. Additional observations, if necessary:

NONE

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V. Reason d statement under Article 35(2) with regard to n velty, inventiv step or industrial applicability; citations and explanations supporting such statement

1. STATEMENT

Novelty (N)	Claims	(Please See supplemental sheet)	YES
	Claims	(Please See supplemental sheet)	NO
Inventive Step (IS)	Claims	(Please See supplemental sheet)	YES
	Claims	(Please See supplemental sheet)	NO
Industrial Applicability (IA)	Claims	(Please See supplemental sheet)	YES
	Claims	(Please See supplemental sheet)	NO

2. CITATIONS AND EXPLANATIONS

Claims 23-25, 27 28, 39-41, 45-50, and 52 lack an inventive step under PCT Article 33(3) as being obvious over FROEHLER et al.(5,645,985). Figures 17B and 17C depict PNA polymeric structure as one option of antisense inhibitory material within the reference. The invention of the reference summarizes the practice of antisense modulation of gene expression in column 10, lines 28-50, inclusive of treatment for disease conditions, of which bacterial diseases are well known conditions. A variety of cells wherein gene expression inhibition may be practiced is described in column 32, lines 5-16, inclusive of bacterial cells. The oligomers of the invention may be made up of 8-40 monomers as described in column 32, lines 31-65. A wide variety of genes may be inhibited as described in the reference in column 33, lines 14-47. Within such gene sequences start codons, CAP sites, etc. may be targeted for inhibition as described in column 43, lines 8-27. Taken as a whole the above summarized descriptions suggest the antibacterial usage of antisense oligomers inclusive of PNA chemical types for inhibition of a variety of bacterial gene expression as desired thus resulting in the instant invention. Thus, it would have been obvious to the practitioner in the art at the time of the instant invention to utilize PNA oligomers for antisense gene inhibition of bacterial genes as instantly claimed.

Claims 31-38 lack an inventive step under PCT Article 33(3) as being obvious over FROEHLER et al.(5,645,985) in view of LEVY (5,650,321). FROEHLER et al. has been summarized above but lacks the inhibition of target genes with antisense oligomers with the determination of its effect on bacteria. LEVY at column 2, lines 15-18, describe the identifying of bacterial genes which are affected antibiotics. This is also summarized more in detail in the reference in column 14, lines 22-51. Isolated genes or segments are suggested and motivated as such expression altering agents in column 3, lines 35-47. Thus, it would have been obvious to the practitioner in the art at the time of the instant invention to perform the instant invention because LEVY describes the identifying of bacterial genes via expression alteration (Continued on Supplemental Sheet.)

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

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VII. Certain defects in the international application

The following defects in the form or contents of the international application have been noted:

The description is objected to as containing the following defect(s) under PCT Rule 66.2(a)(iii) in the form or contents thereof: On page 19, line 19, there is a rectangular symbol after IPTG which is confusingly not filled in. On page 32, lines 24 and 26, the word "varried" is misspelled. On page 34, line 21, a confusing smear is present after "anti-".

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Supplemental Box
(To be used when the space in any f the preceding box s is not sufficient)

Continuation of: Boxes I - VIII

I. BASIS OF REPORT:

This report has been drawn on the basis of the description,
pages, 1-91, as originally filed.
pages, NONE, filed with the demand.
and additional amendments:
NONE

This report has been drawn on the basis of the claims,
numbers, NONE, as originally filed.
numbers, NONE, as amended under Article 19.
numbers, 23-54, filed with the demand.
and additional amendments:
NONE

This report has been drawn on the basis of the drawings,
sheets, NONE, as originally filed.
sheets, NONE, filed with the demand.
and additional amendments:
NONE

V. 1. REASONED STATEMENTS:
The report as to Novelty was positive (YES) with respect to claims 23-54.
The report as to Novelty was negative (NO) with respect to claims NONE.
The report as to Inventive Step was positive (YES) with respect to claims 26, 29, 30, 42-44, 51, 53, and 54.
The report as to Inventive Step was negative (NO) with respect to claims 23-25, 27, 28, 31-41, 45-50, and 52.
The report as to Industrial Applicability was positive (YES) with respect to claims 23-54.
The report as to Industrial Applicability was negative (NO) with respect to claims NONE.

V. 2. REASONED STATEMENTS - CITATIONS AND EXPLANATIONS (Continued):
including inhibition via hybridizable nucleic acids as also described in FROEHLER et al.

Claims 26, 29, 30, 42-44, 51, 53, and 54 meet the criteria set out in PCT Article 33(2)-(3), because the prior art does not teach or fairly suggest the simultaneous application of antibiotic with antisense therapy for bacterial gene inhibition methods. The claims additionally have industrial applicability as control of bacterial growth or viability is a well known desired effect for disease control.

Claims 23-54 meet the criteria set out in PCT Article 33(4) for industrial applicability.

——— NEW CITATIONS ———
US 5,645,985 A (FROEHLER et al.) 08 July 1997, see entire disclosure.

US 5,650,321 A (LEVY) 22 July 1997, see entire disclosure.

Replaced By Article 34

WHAT IS CLAIMED IS:

1. A method of killing or inhibiting growth of bacteria comprising contacting said bacteria with a peptide nucleic acid.

2. The method of claim 1 wherein said peptide nucleic acid is complementary to a region of ribosomal RNA of said bacteria.

3. The method of claim 1 wherein said peptide nucleic acid is complementary to a region of messenger RNA of said bacteria.

4. The method of claim 3 further comprising contacting said bacteria with at least one antibiotic.

5. The method of claim 1 wherein a portion of said peptide nucleic acid is complementary with a region of ribosomal RNA of said bacteria and a further portion of said peptide nucleic acid is complementary with a region of messenger RNA of said bacteria.

6. The method of claim 5 further comprising contacting said bacteria with at least one antibiotic.

7. The method of claim 1 wherein said peptide nucleic acid is from about 5 to about 40 monomer units in length.

8. The method of claim 1 wherein said peptide nucleic acid is from about 6 to about 25 monomer units in length.

9. An antibacterial composition comprising peptide nucleic acid.

10. The antibacterial composition of claim 9 having bacteriostatic properties.

11. The antibacterial composition of claim 9 having bactericidal properties.

12. The antibacterial composition of claim 9 wherein said peptide nucleic acid is targeted to an essential bacterial gene.

13. An antibacterial pharmaceutical composition comprising peptide nucleic acid and a pharmaceutically acceptable carrier or diluent.

14. The antibacterial composition of claim 13 wherein said peptide nucleic acid is targeted to a gene encoding a β-lactamase.

15. The antibacterial pharmaceutical composition of claim 13 wherein said antibacterial pharmaceutical composition further comprises a β-lactam antibacterial agent.

16. The antibacterial pharmaceutical composition of claim 13 wherein said peptide nucleic acid is targeted to an essential bacterial gene.

17. A method of treating a mammal suffering from a bacterial infection comprising administering peptide nucleic acid to the mammal.

18. The method of claim 17 wherein said peptide nucleic acid is complementary to a region of ribosomal RNA of said bacteria .

19. The method of claim 17 wherein said peptide nucleic acid is complementary to a region of mRNA of said bacteria.

20. The method of claim 17 further comprising concurrent treatment with an antibiotic.

21. A method of disinfection comprising,
selecting an object to be disinfected;
contacting said object with peptide nucleic acid; and
rinsing said object with a sterile liquid to remove said peptide nucleic acid.

22. The method of claim 21 wherein said peptide nucleic acid is in the form of a solution and said object is contacted with said solution over substantially all solvent accessible areas of said object.